

REMARKS

The Office Action mailed January 17, 2008, and the prior art applied therein have been carefully reviewed. The claims in the application are now claims 14, 17-21, 24-29, 32-34 and 36-40, and these claims define patentable subject matter warranting their allowance. Applicants accordingly again respectfully request favorable reconsideration and allowance.

Claims 1 and the claims which depend therefrom have been replaced by new claims 36-39 so as to better focus on the structure, with the main claim 36 being presented in Jepson form. In addition, the other independent claims have been slightly restructured.

It should be noted that the hemostatic material according to the present invention does not encompass any embodiment in which both thrombin and fibrinogen are initially held together on a supporting material, but instead encompasses the embodiment, on the one hand, wherein thrombin alone is initially held on a supporting material; and the embodiment, on the other hand, wherein neither thrombin nor fibrinogen are initially held on a supporting material. Thus, the present invention encompasses only these two embodiments. In accordance with present invention, in any case, fibrinogen

is never held on a supporting material either alone or together with thrombin, but is only added immediately prior to use.

As previously emphasized, the substrate used in the present invention is of very substantial importance. Applicants now focus on a bioabsorbable synthetic non-woven fabric made by needle-punching a fabric of polyglycolic acid, noting especially new claims 36-40.

The hemostatic material of the present invention is characterized in that (i) in the first embodiment thrombin alone is held on the supporting material, wherein a non-woven fabric with thrombin held thereon and fibrinogen are separated from each other and fibrinogen is applied to the non-woven fabric only when used; that (ii) in the second embodiment neither thrombin nor fibrinogen are held on a supporting material, wherein both thrombin and fibrinogen are applied to the non-woven fabric only immediately prior to use; and that (iii) in both embodiments a non-woven fabric made of polyglycolic acid such as "Neovéil" manufactured by Gunze Limited is used as the supporting material.

A non-woven fabric made of polyglycolic acid as used in the hemostatic material of the present invention is advantageous in that it has an appropriate elasticity and flexibility to ensure valid sealing as well as excellent

operability and easy handling. Although the cited prior art references disclose that polyglycolic acid may be used as a bioabsorbable material and "paper-like material", they never disclose nor even suggest the effectiveness of a non-woven fabric made of polyglycolic acid.

Besides, the hemostatic material of the present invention is not an integrated sheet material which holds both thrombin and fibrinogen prior to use. Such an integrated sheet material may conveniently and easily be handled, but has a less hemostatic efficacy (see the results of Group 3 in Examples 2 and 3). The reason is that the sheet material is made of collagen, and that thrombin and fibrinogen thereon might have initiated a reaction before actual use within the sheet, and poor hemostatic efficacy resulted. The hemostatic material of the present invention avoided such an integrated sheet material which held both thrombin and fibrinogen together so that better hemostatic efficacy could be provided as shown in Examples 2 and 3.

Claims 1, 5, 6, 21, 24-28 and 32-35 have been rejected as obvious under Section 103 from Greenawalt in view of Ikada. This rejection is respectfully traversed.

The Examiner alleges that although Greenawalt's product is described as "paper-like material", it is made of

polyglycolic acid (PGA), which would provide sufficient elasticity and flexibility as evidenced by Ikada and therefore the PGA fabric of Greenawalt would have inherent elasticity and flexibility to be formed into any shape. However, it should be noted that the PGA material disclosed in Greenawalt is a paper-like material prepared merely by dissolution and subsequent pressing, i.e. a paper making process (cf. e.g. Example 2), such paper-like material being quite distinct from a non-woven fabric of the present invention which is prepared by needle-punching fabric made of PGA.

The Examiner states that "Greenawalt et al teach a two component system of fibrin glue, which comprises thrombin and fibrinogen separately and used together prior to application (see column 1, lines 19-38)" at page 5, the last paragraph. However, it should be noted that this teaching is made in association with the conventional two component system of fibrin glue with no use of a sheet of any kind. Greenawalt discloses a sheet preparation as an improvement from such non-sheet fibrin glue. Greenawalt discloses, as such a sheet preparation, either PGA/thrombin/fibrinogen (i.e. integrated sheet material) or PGA/thrombin, but does not disclose or suggest that PGA/thrombin and fibrinogen are separated from each other and combined together only when put to use.

The hemostatic material of the present invention is not an integrated sheet material which holds both thrombin and fibrinogen, but instead is such that thrombin alone is held on the supporting material or neither thrombin nor fibrinogen are held on the supporting material to thereby exert a much better hemostatic efficacy as compared to the conventional integral sheet preparation.

Accordingly, even if it were obvious to combine the references as proposed, respectfully not admitted, the reconstructed Greenawalt would not correspond with the claimed subject matter.

Withdrawal of the rejection is in order and is respectfully requested.

As regards claim 28, the examiner appears to be taking the position that lyophilizing can be ignored because it is a process limitation. This is not correct! Applicants do not dispute that determination of patentability is based on the product itself, but applicants respectfully point out that the process by which the product is made can characterize the nature of the product itself and thus serve to distinguish the product. In this regard, attention is respectfully invited to *In re Luck et al*, 177 USPQ 523, 525 (POBA 1973), where the Board stated:

As for the method of application, it is well established that product claims may include process steps to wholly or partially define the claimed product. See *In re Brown...* 173 USPQ 685, 688 (1972), and the cases cited therein. To the extent these process limitations distinguish the **product** over the prior art, they must be given the same consideration as traditional product characteristics. [Emphasis in original]

There should be no doubt whatsoever that a product which has been lyophilized is different in character from a product which has not been lyophilized.

Therefore, even if claim 28 is deemed to contain a process limitation (or any other claim for that matter), the process limitation must be given consideration to the extent that the process changes the product.

At the top of page 8 of the Office Action, the rejection expresses the view, as understood, that the "paper-like material" of Greenawalt "would have inherent elasticity and flexibility to be formed into any shape." Respectfully, this makes no sense to applicants. While it is true that paper is flexible in one sense, normal paper clearly does not have elasticity, and cannot be formed into any shape.

The law on inherency is very clear. For inherency to apply in a rejection under Section 102 or 103, the missing feature must be necessarily present. As stated in *Ex parte Levy*, 17 USPQ 2d 1461, 1463-64 (BPAI 1990):

In relying on the theory of inherency, the examiner must provide a basis of fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic **necessarily** flows from the teaching of the applied prior art. [citations omitted; emphasis in the original]

Please also see *In re Robertson*, 49 USPQ2D 1949, 1951 (Fed. Cir. 1999) :

Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. [citations omitted]

As Greenawalt does not disclose applicants' substrate and as it cannot be said with reasonable certainty that the paper-like material of Greenawalt possesses elasticity (and indeed the opposite quite clear), it cannot be validly said that Greenawalt shows or make obvious the claimed feature in question.

Claims 1, 5, 6, 14, 17-21, 24-29 and 32-35 have been rejected as obvious under Section 103 from newly cited and applied Sugitachi et al USP 4,265,233 (Sugitachi) in view of newly cited and applied Roth USP 3,937,223 (Roth) further in view of Greenawalt. This rejection is respectfully traversed.

The Examiner alleges that Sugitachi teaches an absorbable material such as PGA comprising thrombin, and a process of making such. However, although Sugitachi discloses a method for fixing blood coagulation factors on an absorbable

material, the absorbable material used in the working examples is a gauze (Example 2) or a gelatin sponge (Example 6).

Although the use of PGA material is described in Example 7, it is a braided suture of PGA, but not a non-woven fabric.

Besides, Sugitachi relates to a wound protecting and healing material which is different from a hemostatic material. Thus, the purpose for use of the preparation per se is different between the present invention and Sugitachi.

The Examiner alleges that Roth teaches a hemostatic felt made of PGA and PGA felt (non-woven fabric) having flexibility to conform readily to the surface of a bleeding wound, and it would therefore have been obvious for the person of ordinary skill in the art to replace the absorbable material of Sugitachi with PGA felt of Roth. But this is not what applicants claim. Moreover, it should be noted that Roth aimed at hemostasis through a fibrous structure (felt) per se of a bioabsorbable material, and also disclose processing thereof.

Roth's teaching is irrelevant since it is an invention of a "physical structure" where hemostasis may be achieved by appropriately receiving blood, which is essentially different from the present invention (and from Sugitachi) where hemostasis may be attained by a blood coagulation reaction to be artificially induced on a

supporting material (a non-woven fabric made of PGA). Thus, it would not be pertinent or obvious to combine Sugitachi with the teaching of Roth.

Besides, it appears that the Examiner may have rejected on the assumption that "stopping bleeding" and "wound healing" are the same (page 9, 5th paragraph). However, "stopping bleeding" (hemostasis) and "wound healing" are the two concepts quite distinct from each other. This would be apparent from the disclosure of Sugitachi per se, namely a wound healing material according to Sugitachi has FXIII fixed thereon but lacks fibrinogen. This is because fibrin formed from a high level of fibrinogen would be risky as deterring wound healing, and rather such a level of fibrinogen as in patient blood would be preferable.

The gist of the invention and thus the teaching of Sugitachi lies in fixation of FXIII but not thrombin on an absorbable material since FXIII is known to be a factor promoting wound healing. Thus, thrombin in Sugitachi should be considered a rather accessory element and is expected to promote efficient activation of FXIII.

The Examiner states that with regard to the elastic property of the hemostatic material of the present invention, the hemostatic felt made of PGA comprising thrombin taught by Sugitachi in view of Roth would have inherently possessed the

same property as the claimed invention because the material of the reference is considered the same or substantially identical to the claimed invention (paragraph bridging pages 11 and 12). However, the Examiner's position is not pertinent because such elastic property would not be determined solely by the sameness of the material but rather would vary depending on composition or amount of each of a protein, an additive and the like even if the same sheet material were to be processed.

Greenawalt has been discussed above and previously. It does not solve the aforementioned problem of Sugitachi and Roth being incompatible and it is not obviously combinable with Roth for the same reasons as pointed out above with respect to Roth being not combinable with Sugitachi. Moreover, even if the references were obviously combinable, they do not lead to the use of a non-woven fabric of PGA, an important characteristic of the present invention.

Withdrawal of the rejection is in order and is respectfully requested.

Applicants assert with respect that all issues raised in the Official Action have been addressed above in a manner that should lead to patentability of the present application. Favorable consideration and early formal allowance are respectfully requested.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant

By



Sheridan Neimark

Registration No. 20,520

SN:jnj
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\A\AOYB\UCHIDA9\PTO\2008-7-17AMD.docS